Uptake of hepatitis C specialist services and treatment following diagnosis by dried blood spot in Scotland

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Abstract

Background

Dried blood spot (DBS) testing for hepatitis C (HCV) was introduced to Scotland in 2009. This minimally invasive specimen provides an alternative to venipuncture and can overcome barriers to testing in people who inject drugs (PWID).

Objectives

The objective of this study was to determine rates and predictors of: exposure to HCV, attendance at specialist clinics and anti-viral treatment initiation among the DBS tested population in Scotland.

Study design

DBS testing records were deterministically linked to the Scottish HCV Clinical database prior to logistic regression analysis.

Results

In the first two years of usage in Scotland, 1322 individuals were tested by DBS of which 476 were found to have an active HCV infection. Linkage analysis showed that 32% had attended a specialist clinic within 12 months of their specimen collection date and 18% had begun anti-viral therapy within 18 months of their specimen collection date. A significantly reduced likelihood of attendance at a specialist clinic was evident amongst younger individuals (<35 years), those of unknown ethnic origin and those not reporting injecting drug use as a risk factor.

Conclusion

We conclude that DBS testing in non-clinical settings has the potential to increase diagnosis and, with sufficient support, treatment of HCV infection among PWID.

Background

In Scotland, 0.8% of the population aged 15-59 years had been diagnosed with hepatitis C virus (HCV) antibodies by the end of 2012 [1]. The majority of these infections occur in individuals with a history of injecting drug use [2] and recent estimates suggest that around half of people infected with HCV remain undiagnosed [1]. To tackle the epidemic of HCV in Scotland, the Hepatitis C Action Plan for Scotland was launched in September 2006 [3]. In its initial Phase (September 2006 – March 2008) the Action Plan identified poor venous access amongst people who inject drugs (PWID), along with a shortage of trained phlebotomists, and the long interval between testing and return of results, as barriers to testing and diagnosis of HCV in this population [4]. Dried blood spots (DBS), drops of whole blood from a finger prick dried onto filter paper, provide an alternative to whole blood specimens collected by venipuncture and can overcome the majority of barriers to HCV testing outlined above [5,6,7,8]. As a result of the Action Plan, DBS testing for HCV diagnosis was introduced in Scotland in May 2009. Now that DBS testing is well established in Scotland, the outcomes of DBS testing are quantifiable to give a better understanding of the utility of the DBS approach.

Objectives

The objective of this study was to determine the proportion of those tested by DBS in Scotland who had been exposed to HCV; of those diagnosed as being currently infected with HCV the proportion attending a specialist clinic and, of those, the proportion who were initiated on anti-viral treatment. Epidemiological information

collected alongside the DBS specimens is also analysed to identify predictors of exposure, attendance and treatment initiation amongst this population.

Study Design

Data Sources and Linkage

The Scottish Hepatitis C Clinical Database, held at Health Protection Scotland (HPS), contains clinical follow-up data for HCV-infected patients attending 17 specialist clinics across Scotland. These data include attendance dates, treatment episodes, demographic, clinical, virological, and patient identifiers (date of birth, sex, surname Soundex (a consonant-only phonetic encoding), and forename initial). Data were restricted to individuals on the database on 31 December 2012 and at this date the database contained records for 14,298 individuals with sufficient identifiers for linkage.

HPS also maintains records on all DBS testing in Scotland since May 2009. The DBS database contains information on dates and result(s) of HCV antibody and reverse transcriptase polymerase chain reaction (RT-PCR) testing, source, ethnicity, risk activitie(s), length of injecting career and limited identifying information (i.e., date of birth, sex, surname Soundex and forename initial). On 31 December 2010 this database comprised records for 1448 specimens relating to 1322 individuals.

Records from the DBS database (up to 31 December 2010) were deterministically linked to individuals on the HCV Clinical database (to 31 December 2012); a complete match on surname Soundex, gender, DOB, and first initial was required for a successful link.

Data Analysis

Three main outcomes were analysed: (a) anti-HCV positivity amongst all individuals tested by DBS for HCV since the inception of the DBS testing programme in Scotland (May 2009) to 31 December 2010, (b) first clinic attendance amongst all chronically HCV-infected persons recorded as being tested by DBS for HCV infection between May 2009 and 31 December 2010 and (c) initiation on antiviral therapy amongst the chronically HCV-infected patients attending a specialist clinic. Univariate and multivariate logistic regression modelling was used to examine the association between the covariates sex, age at diagnosis (grouped into < 35years, ≥ 35years), ethnicity (White, Unknown/Non-white), Source of DBS (Community Addiction Team/Harm Reduction, Other) and time since onset of injecting ($\leq$10years, $>$ 10years, Not Known (PWID), Non-PWID) and the outcomes: 'HCV antibody positive' (Table 1), 'first clinic attendance within 12 months of diagnosis by DBS' (Table 2) and 'initiation on antiviral therapy within 18 months of DBS specimen collection' (Table 3). For the latter analysis the variable 'Risk Factor' (Current PWID, Past PWID, Non-PWID/Unknown) was also included. For the Risk Factor variable data collected on length of injecting career (including age of first and last injection) was used, where available, to categorise individuals as past PWID and present PWID, with any individual giving a date of last injecting drug use as five or more years prior to the DBS specimen collection date classified as a past PWID.

All analysis was carried out in R 3.0.1 [8]. Exact p-values are provided except where $P< 0.001$.

Results

In 2009/10 DBS specimens were collected from 1322 individuals in Scotland for HCV screening. Of these individuals 55% (n=728) were seropositive for antibody to HCV, and approximately two-thirds (65.4% (n=476)) had an active HCV infection (Figure 1). Table 1 presents characteristics of the overall study sample, according to HCV antibody prevalence. The majority (70%) were males, although HCV antibody prevalence in both sexes was equal at 55%. The average age of all DBS tested individuals was 36, with 45% of individuals falling into the < 35yrs age category and 55% into the ≥ 35yrs category. Antibody prevalence was significantly higher in the older age category compared to the younger; 64% (95% CI: 60 – 67%) and 45% (95% CI: 41 – 49%) respectively. White was the main ethnicity (82.8%), the remainder being of unknown (16.5%) or non-white (0.7%) ethnicity. Most individuals (89.3%) were tested in a community addiction team or harm reduction setting as opposed to other settings (hospital (3.8%), GP (1.7%), prison (0.6%) or private (4.6%)).

Odds of HCV antibody

Multifactorial logistic regression analysis found age to be related to odds of antibody positivity, with those aged ≥ 35 years significantly more likely (AOR=1.93, 95% CI:1.51 – 2.47) than those aged < 35 years to be antibody positive. The adjusted odds ratio of ethnicity was also positively associated with prevalence. Individuals who were recorded as being of white ethnic origin being more likely (AOR=2.00, 95% CI: 1.42 – 2.85) to be antibody positive as those of unknown/non-white ethnic origin.

PWID are well known to be at increased risk of infection with hepatitis C, particularly those with longer injecting histories. The majority of individuals (85.6%) tested by DBS reported being/having been a PWID; those who did not report injecting drug use as a risk factor were less likely to be antibody positive (AOR=0.28, 95% CI: 0.17 – 0.39) than those who had commenced injecting in the previous ten years. There was a marked increase in prevalence between individuals who had injected for 10 years or less (46.8%) and individuals with injecting histories of over 10 years (80.0%). This translated into a 3.6-fold increased odds of HCV exposure for the individuals with injecting histories of over a decade (AOR=3.58, 95% CI: 2.36 – 5.45) in the adjusted analysis. Finally, although not significant in the multifactorial analysis, individuals tested in a community addiction clinic/harm reduction setting (n=1180) were more likely (OR=1.84. 95% CI: 1.30 – 2.63) to be positive for antibody to HCV as those tested in other settings in the univariate analysis (Table 1).

Attendance at Specialist Hepatitis Clinics within 12 months of DBS specimen.

Of the 728 individuals known to be antibody positive there were 476 (65.4%) individuals with an active HCV infection as confirmed by RT-PCR. Linkage of these individuals to the Hepatitis C Clinical Database showed that 202 (42.4%) had ever attended a specialist hepatitis clinic, and 31.9% (n=152) within 12 months following collection of their DBS specimen (Figure 1). For 7.8% (n=37) of individuals a date of attendance prior to the DBS specimen date was also found.

Univariate analysis did not show any significant relationship between the likelihood of attendance at a specialist hepatitis clinic within the twelve months following diagnosis by DBS and any of the examined variables. However, multifactorial

logistic regression found a significant relationship between age, risk factor status and ethnicity and attendance at a specialist clinic within 12 months. Individuals aged 35 or older were more likely (AOR=1.49, 95% CI: 1.05-2.13) than those aged <35 years to attend a treatment clinic within 12 months of DBS diagnosis. Individuals who were recorded as being of a white ethnic background were also more likely (AOR=2.85, 95% CI: 1.57-5.58) to attend a clinic within 12 months as those of a unknown/non-white ethnic background, and there was also a significantly reduced likelihood (AOR=0.32, 95% CI: 0.13 – 0.71) of attendance at a clinic within 12 months for individuals with a non-PWID risk factor (Table 2).

Initiation on anti-viral therapy within 18 months of DBS specimen date

Of the 202 individuals recorded as attending a specialist hepatitis clinic following collection of a DBS specimen in 2009/10, 66 individuals (32.7%) were recorded beginning anti-viral therapy up to the end of 2012. For 18.3% (n=37) of individuals anti-viral therapy was commenced within 18 months of having the DBS specimen collected (Figure 1). Following logistic regression analysis there was no significant association with the likelihood of receiving treatment within 18 months post DBS testing and any of the variables examined in this analysis (Table 3).

Discussion

Previous studies have demonstrated the effectiveness of DBS in terms of test uptake amongst PWID [5,6,7,8]. To our knowledge, this is the first study to report on the performance of DBS testing in terms of attendance at specialist clinics and treatment initiation. Overall, we found that of the 476 individuals with active HCV infection, tested by DBS in 2009 and 2010, 31.9% had attended a specialist clinic within 12 months of their specimen collection date and, of these, 18.3% had begun anti-viral therapy within 18 months of their specimen collection date.

To understand how these figures compare to overall HCV diagnosis in Scotland we can relate our findings to a recent analysis which reviewed similar outcomes, across an overlapping time period, in all new HCV diagnoses in Scotland from 1996 onwards. The authors report that, of the 1364 individuals newly diagnosed with chronic HCV in Phase II of the Scottish Hepatitis C Action Plan (1 May 2008 to 31 December 2010), 44.5% attended a specialist hepatitis clinic within 12 months of being diagnosed and 32% were initiated on anti-viral treatment within the 12 month period following first clinic attendance [10]. Comparing these figures shows that attendance at specialist hepatitis clinics is lower in the DBS tested population at the 12 month follow-up point (31.9%) and, although not directly comparable, there also appear to be lower rates of initiation onto anti-viral therapy in the DBS tested population. The populations are not entirely analogous, most notable is that the McDonald et al (2013) study included only new HCV diagnoses whereas this analysis included all diagnoses; among whom there was evidence of prior engagement with specialist services (Figure 1). Since prior knowledge of HCV status may influence

193 the probability of attendance and treatment this may account for some of the variation
194 between the studies. Finally, in our population, of those chronically infected with
195 HCV, 95.4% reported having been/being a PWID and 92.6% were tested at a
196 drug/counselling clinic, compared to 41.9% and 9.7% of the newly diagnosed
197 population. Thus the DBS diagnosed population may well represent a more chaotic
198 group of individuals, involving those who continue to use and inject drugs, which
199 would help to explain the poorer attendance and treatment outcomes amongst this
200 population. Treatment of current PWIDs is still considered problematic by some
201 medical professionals due to concerns over adherence to treatment regimes, medical
202 and psychiatric co-morbidities, psychosocial issues and risk of re-infection [11].
203 However, there is growing evidence to show that, given adequate support, good
204 treatment outcomes can be achieved among people who continue to inject drugs
205 [12,13].
206
207 Looking within our DBS-tested population, logistic regression analysis showed that
208 attendance at specialist hepatitis clinics within 12 months of the DBS specimen
209 collection date was significantly reduced amongst individuals aged less than 35 years
210 and those of unknown/non-white ethnic origin. The significance of the latter finding
211 is unclear as the majority (>98%) of individuals in this category were of unknown
212 ethnicity. We also found that those in the non-PWID risk factor category are
213 significantly less likely to attend a clinic within 12 months of their DBS collection
214 date, despite being chronically infected with HCV. The basis of this difference is
215 unclear but may reflect the high proportion of PWID in our study and the emphasis of
216 this risk factor amongst healthcare professionals working in DBS testing settings.
217 Awareness of these demographic trends amongst healthcare professionals may enable

targeted post-test discussion. This analysis did not find any significant association between the variables examined and the likelihood of treatment initiation which may be due to the small sample size and, additionally, our analysis did not have the scope to include the physical, psychological and social factors involved in the decision to treat individuals, and/or willingness to undergo treatment, which have been found to be significant in other studies [14, 15,16].

DBS testing was recently estimated to be cost-effective in addiction services settings in the UK at an estimated £14,600 per quality adjusted life year (QALY) gained [17]. The model was based on 35% of PWID being successfully referred from testing services to secondary care and 5.5% of referred PWID being treated within 2 years. The latter variable was based on the assumption that 1% of infected PWID are treated within 2 years, or 5.5% of those who attended referral. The authors note that the treatment parameter was a critical factor in assessing the cost-effectiveness of DBS testing since higher treatment rates prevent disease transmission thereby increasing the cost-effectiveness of case-finding interventions. Whilst referral rates in our study are similar to those estimated in the model, we have found a much higher proportion of individuals in secondary care being treated; up to a third within 4 years of their DBS specimen and 18% within 18 months of their DBS specimen. Although a proportion of our sample were determined to be past-PWID, for whom treatment rates are higher, 86.2% of the PWID with an active HCV infection had injected within the past five years. As such these findings have great bearing on the cost-effectiveness of DBS testing which was estimated to drop to £4500 per QALY if 50% of referred PWID initiated treatment within 2 years [17].

Our findings are further evidence of the utility of DBS testing in reaching the populations most at risk from HCV infection and engaging them with specialist hepatitis services. Recent advances in HCV treatment, with the introduction of triple therapy as a standard treatment regime, has significantly improved the rates of sustained virological response [18] and the prospect of interferon-free treatment regimens makes the possibility of an all-oral therapy for HCV conceivable [19,20]. Such advances will make treatment a more tolerable therapy and also open the possibility of treatment in the community setting; both of which may facilitate greater uptake in the DBS-tested population in the future. In anticipation of these changes in HCV therapy, and the accompanying possibilities for treatment expansion, the use of DBS should be supported and expanded to maximise engagement with this population.

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Conflicts of Interest

Funding: This work was funded by The Scottish Government as part of the Hepatitis C Action Plan for Scotland.

Competing interests: Peter Hayes has received payment from Gilead , MSD and Jannsen and Roche

Ethical approval: Epidemiological data is collected on the laboratory request form and returned along with the dried blood spot specimen to the testing laboratories. All data is handled in accordance to local NHS governance regulations. DBS specimens are always collected with informed consent and the patient is under no obligation to supply any further information along with the specimen. Patients are made aware that any epidemiological information they do provide is held as anonymous surveillance data and will be used for auditing, public health monitoring etc.

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